

Reply dated June 16, 2004

Response to Office Action dated January 16, 2004

**AMENDMENTS TO THE CLAIMS:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

1. (currently amended) A nano-calcium ~~phosphates/collagen~~ phosphate/collagen composite, comprising collagen molecules and nano-calcium ~~phosphates~~ phosphate, wherein said composite ~~in microstructure level is comprises~~ agglomerated particles having a diameter of 5-50 microns, ~~and in nanostucture level is of~~ ~~wherein the agglomerated particles comprise a multiple laminar structure having periodic periodically repeated units, each periodic periodically repeated unit having a thickness of 10-15 nm and consisting of a layer of nano calcium~~ calcium phosphates and a layer of collagen.

2. (original) The nano-calcium phosphates/collagen composite of claim 1, wherein the collagen is type I collagen.

3. (currently amended) The nano-calcium phosphates/collagen composite of claim 1, wherein the weight ratio of nano-calcium phosphates to collagen molecules is between about 2.2 to about 2.8.

4. (currently amended) A process for preparing the composite of claim 1, comprising the following steps:

(a) dissolving collagen gel in acetic acid, then adding aqueous solutions of sodium phosphate and  $\text{CaCl}_2 \cdot 6\text{H}_2\text{O}$  calcium chloride, wherein the weight ratio of Ca:P is between 1:1 to 1.67:1, ~~and the amounts of collagen and minerals used are corresponding to those in the natural bone;~~

(b) adding in drops sodium hydroxide solution until the calcium phosphates start to co-precipitate with collagen;

(c) maintaining the solution of step (b) at neutral pH and incubating the solution at 30° for 1~5 days; and

(d) harvesting the composite by centrifugation, freeze-drying and grinding into fine powder.

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5. (currently amended) A porous bone substitute or tissue engineering scaffold, comprising a complex of the composite of claim 1 and poly(lactic acid) or poly(lactic acid-co-glycolic acid), wherein the weight ratio of said composite and poly(lactic acid) or poly(lactic acid-co-glycolic acid) is between about 3:7 to about 1:1, the porosity is ~~ever~~ about 70% or more and the pore size is about 100-500 microns.

6. (original) The scaffold of claim 5, further comprising noncollagenous bone matrix proteins, such as bone morphogenetic protein and bone growth factors as well as multiple glycoproteins that can promote cell attachment and spreading.

7. (currently amended) A process for preparing a porous bone substitute or tissue engineering scaffold, comprising the following steps:

(a) dissolving poly(lactic acid) or poly(lactic acid-co-glycolic acid) in dioxane to a final concentration of about 2.5-15%(w/v), then stirring the solution gently for about 4 to 6 hours;

(b) adding the nano-calcium ~~phosphates/collagen~~ phosphate/collagen composite powder of claim 1 with [[the]] a ratio of composite: poly(lactic acid) or poly(lactic acid-co-glycolic acid) being of about 3:7 to 1:1;

(c) ultrasonicating the solution of step (b), then pouring into a mold and freezing at a temperature between 0 to -20° overnight; and

(d) transferring the frozen molded scaffold into a freeze drying machine to remove dioxane ~~erystals~~.

8. (original) A porous bone substitute scaffold obtained by the process of claim 7.

9-10. (cancelled)

11. (previously presented) A method of treating bone defect or bone fracture, said method comprising administering to said bone defect or bone fracture an effective amount of a scaffold according to claims 5, 6 or 8.

12. (previously presented) A method of culturing osteocytes, said method comprising providing an effective amount of a scaffold according to claims 5, 6 or 8 for culturing osteocytes.